



Docket No. 0575/59154-A/JPW/GJG/AN

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Virginia W. Cornish  
Serial No. : 09/768,479  
Filed : January 24, 2001  
For : IN VIVO SCREEN FOR ENZYMATIC ACTIVITY

1185 Avenue of the Americas  
New York, New York 10036  
June 29, 2001

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicant would like to direct the Examiner's attention to the following disclosures, which are listed on Form PTO-1449 (**Exhibit A**). Copies of the disclosures listed below as items 1-34 are attached hereto as **Exhibits 1-34**, respectively:

1. U.S. Patent No. 5,736,343 (Landry) issued April 7, 1998 (**Exhibit 1**);
2. U.S. Patent No. 5,468,614 (Fields et al.) issued November 21, 1995 (**Exhibit 2**);
3. U.S. Patent No. 5,314,817 (Schultz, P.) issued May 24, 1994 (**Exhibit 3**);

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4. U.S. Patent No. 5,194,594 (Kwawli et al.) issued March 16, 1993 (**Exhibit 4**);
5. PCT International Application Publication No. WO 99/10510 (Natesan et al.) published March 4, 1999 (**Exhibit 5**);
6. PCT International Application Publication No. WO 99/10508 (Natesan et al.) published March 4, 1999 (**Exhibit 6**);
7. PCT International Application Publication No. WO 98/13353 (Whitney et al.) published April 2, 1998 (**Exhibit 7**);
8. PCT International Application Publication No. WO 97/31113 (Rickles et al.) published August 28, 1997 (**Exhibit 8**);
9. PCT International Application Publication No. WO 96/30540 (Tsien et al.) published October 3, 1999 (**Exhibit 9**);
10. European Patent Application Publication No. EP 0 742 015 (Kadow et al.), published November 13, 1996 (**Exhibit 10**);
11. Austin DJ, et al. Proximity versus allostery: the role of regulated protein dimerization in biology. 1994. Chem Biol. 1(3): 131-6 (**Exhibit 11**);
12. Belshaw PJ, et al. Controlling protein association and subcellular localization with a synthetic ligand that induces heterodimerization of proteins. 1996. Proc. Natl

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Acad Sci USA 93(10):4604-7 (**Exhibit 12**);

13. Belshaw PJ, et al. Controlling programmed cell death with a cyclophilin-cyclosporin-based chemical inducer of dimerization. 1996. Chem. Biol. 3:731-738 (**Exhibit 13**);
14. Choi J, et al. Structure of the FKBP-12-Rapamycin complex interacting with the binding domain of human FRAP. 1996. Science 273(5272):239-42 (**Exhibit 14**);
15. DeGrado WF, et al. Screening, selection and design: standing at the crossroads in three dimensions. 1997. Current Opinion in Structural Biology 7:455-456 (**Exhibit 15**);
16. Diver SR, et al. Single-step synthesis of cell-permeable protein dimerizers that activate signal transduction and gene expression. 1997. J. Am. Chem. Soc. 119, 5106-5109 (**Exhibit 16**);
17. Ho SN, et al. Dimeric ligands define a role for transcriptional activation domains in reinitiation. 1996. Nature. 382(6594):822-6 (**Exhibit 17**);
18. Holsinger LJ, et al. Signal transduction in T lymphocytes using a conditional allele of Sos. 1995. Proc. Natl. Acad. Sci. USA 92:9810-9814 (**Exhibit 18**);

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19. Hung DT, et al. Understanding and controlling the cell cycle with natural products. 1996. Chem. Biol. 3:623-639 (Exhibit 19);
20. Klemm JD, et al. Dimerization as a regulatory mechanism in signal transduction. 1998. Annu. Rev. Immunol. 16:569-92 (Exhibit 20);
21. Liberles SD, et al. Inducible gene expression and protein translocation using nontoxic ligands identified by a mammalian three-hybrid screen. 1997. Proc. Natl. Acad. Sci. USA 94(15):7825-7830 (Exhibit 21);
22. Licitra EJ, et al. A three-hybrid system for detecting small ligand-protein receptor interactions. 1996. Proc. Natl. Acad. Sci. USA 93:12817-12821 (Exhibit 22);
23. Pedersen H, et al. A method for directed evolution and functional cloning of enzymes. 1998. Proc. Natl. Acad. Sci. USA 95:10523-10528 (Exhibit 23);
24. Pruschy MN, et al. Mechanistic studies of a signaling pathway activated by the organic dimerizer FK1012. 1994. Chem. Biol. 1:163-172 (Exhibit 24);
25. Schreiber SL. Chemical genetics resulting from a passion for synthetic organic chemistry. 1998. Bioorganic & Medicinal Chemistry 6:1127-1152 (Exhibit 25);

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26. Spencer DM , et al. Controlling signal transduction with synthetic ligands. 1993. Science 262(5136):1019-1024 (Exhibit 26);
27. Spencer DM, et al. Functional analysis of Fas signaling in vivo using synthetic inducers of dimerization. 1996. Curr Biol. 6(7):839-47 (Exhibit 27);
28. Spencer DM, et al. A general strategy for producing condition alleles of Src-like tyrosine kinases. 1995. Proc. Natl. Acad. Sci. 92:9805-9809 (Exhibit 28);
29. Stockwell BR, et al. TGF-beta-signaling with small molecule FKBP12 antagonists that bind myristoylated FKBP12-TGF-beta type 1 receptor fusion proteins. 1998. Chem Biol. 5(7):385-95 (Exhibit 29);
30. Stockwell BR, et al. Probing the role of homomeric and heteromeric receptor interactions in TGF-beta signaling using small molecule dimerizers. 1998. Curr Biol 8(13):761-70 (Exhibit 30);
31. Winkler T, et al. Confocal fluorescence coincidence analysis: An approach to ultra high-throughput screening. 1998. Proc. Natl. Acad. Sci. USA 96:1375-1378 (Exhibit 31);
32. Yang J, et al. Small-molecule control of insulin and PDGF receptor signaling and the role of membrane attachment.

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1997. Curr. Biol. 8:11-18 (**Exhibit 32**);

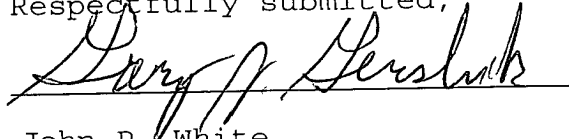
33. Zlokarnik G, et al. Quantitation of transcription and clonal selection of single living cells with beta-lactamase as reporter. 1998, Science 279(5347):84-8 (**Exhibit 33**); and

34. Search Report dated May 14, 2001 corresponding PCT International Application No. PCT/US01/02285 (**Exhibit 34**).

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

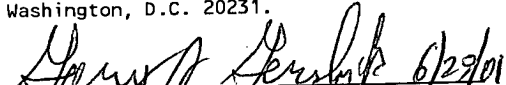
No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. If any such fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.



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